**U. S. Food and Drug Administration**
**Office of Public Affairs**
**Fact Sheet**
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# FOLIC ACID FORTIFICATION

(See updated information on folic acid, FDA Consumer, February 1999)

## Background:

The U.S. Public Health Service recommended in September 1992 that all women of childbearing age consume 400 micrograms (ug) of folic acid daily to reduce their risk of having a pregnancy affected with spina bifida or other neural tube defects. Folic acid is a B vitamin. For women, this amount of folic acid on a daily basis spina bifida or anencephaly, both of which are neural tube defects (NTDs) in the baby.

PHS suggested several approaches by which this level could be reached:

- Improved dietary habits
- Fortification of the U.S. food supply
- Daily use of folic acid supplements by women throughout their childbearing years.

## FDA Action:

In keeping with the recommendations of PHS and the FDA Food Advisory Committee called to study these issues, the Food and Drug Administration is requiring that folic acid be added to specific flour, breads and other grains. These foods were chosen for fortification with folate because they are staple products for most of the U.S. population, and because they have a long history of being successful vehicles for improving nutrition to reduce the risk of classic nutrient deficiency diseases.

These fortified foods include most enriched breads, flours, corn meals, rice, noodles, macaroni and other grain products.

**Under the terms of the new rule:**

- Fortification levels will range from 0.43 milligrams to 1.4 mg per pound of product.
- Fortification of grain products at these levels will allow the daily intake from all sources to remain below the recommended upper limit of 1 mg per day.
- The amount of folic acid that will be consumed through foods fortified at these levels is considered safe for all population (age/gender) groups.
- Manufacturers will be allowed to make claims on the labels that the fortified products contain folic acid and that adequate intake of the nutrient may reduce the risk of neural tube defects.

FDA also emphasizes that adequate levels of folic acid, in the form of folate, can be obtained by eating natural sources such as:

- Leafy dark green vegetables
- Legumes (dried beans and peas)
- Citrus fruits and juices
- Most berries

In addition, women can assure adequate intake by taking dietary supplements containing folic acid.

The new rule takes account of the finding in PHS' recommendation that total folate consumption should be kept under 1 mg per day. This is because higher intake may complicate the diagnosis of pernicious anemia, one form of vitamin B12 deficiency, which especially affects older people.

## Neural Tube Defects:

Neural tube defects, including spina bifida and anencephaly, are a common birth defect.

- Approximately 2,500 infants are born each year in the U.S. with an NTD. About half this number are though to be related to inadequate folate intake by the mother. Other NTDs have different causes that are not well understood.

- Spina bifida is a condition in which the spinal cord is exposed. A majority of babies born with spina bifida grow to adulthood with varying degrees of disability, ranging to problems with bowel and bladder control, and paralysis. Many may require a series of operations and other treatments.

- In anencephaly, infants die shortly after birth because most or all of the brain is absent.

Since NTDs develop very early in pregnancy (18-30 days after conception), often before a woman knows she is pregnant, it is essential that adequate intake of folic acid be maintained throughout the childbearing years.

Women who have had a prior NTD-affected pregnancy are at high risk of having a subsequent affected pregnancy. When these women are planning to become pregnant, they should consult their physicians for advice.

## Pernicious Anemia & Recommended Daily Limit:

Because the effects of high intakes of folic acid are not well known, but do include complicating the diagnosis of vitamin B12 deficiency, care should be taken to keep total folate consumption under 1 mg per day, except under the supervision of a physician.

- About 10 to 20 percent of the elderly are diagnosed as having low vitamin B12 levels.

- The effects of folic acid at levels between 1 and 5 mg are not well known, but include complicating the diagnosis of vitamin B12 deficiency.

- Among persons with pernicious anemia, one form of vitamin B12 deficiency, adverse effects have been reported with daily intakes of 5 mg folic acid and above.

• Because FDA has a mandate to set fortification levels that are safe for all population groups, lack of long term data makes it impossible to conclude that continuous intakes of 1 mg or more daily would be safe.

The FDA rule is designed to keep total folic acid intake under the 1 mg level.

### History of Food Fortification:

Addition of iodine to salt was one of the earliest successful fortification programs. Iodine fortification was initiated in the U.S. in 1924 to prevent goiter, cretinism and other symptoms of severe iodine deficiency.

In the early 1930s, vitamin D was first added to cow's milk to aid in absorption of calcium and phosphorus, preventing development of rickets.

In 1938, voluntary enrichment of flours and breads was initiated to prevent the development of deficiency diseases in the general population. Enrichments included thiamin for beriberi, niacin for pellagra, riboflavin essential for proper functioning of vitamin B6 and niacin, and iron for iron deficiency anemia. Mandatory requirements were effective in 1943.

There are various other fortification requirements to enhance the quality of food such as vitamin A added to low and nonfat cow's milk and certain other dairy products, and lysine added to certain corn products to enhance protein quality.

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The 1994 FDA Consumer magazine article reprinted below provides additional information on folic acid and neural tube defects.

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# FDA Proposes Folic Acid Fortification

### by Rebecca D. Williams

The message to pregnant women is clear. A little investment in nutrition now pays off richly in your baby's health later.

For that reason, the Food and Drug Administration proposed last October that all bread and grain products be fortified with folic acid, one of the B vitamins. Just 0.4 milligrams (mg) of the nutrient every day can greatly reduce the risk of neural tube defects, which affect the brain and spinal cord.

Folate is in many healthful foods. (Folate and folic acid are interchangeable terms. Folic acid is the synthetic form of folate, which is found naturally in some foods.) A bowl of lentil soup or fortified breakfast cereal, a large spinach salad, or a tall glass of orange juice will put a woman well on her way to 0.4 mg of folic acid.

The tricky part is that neural tube defects occur in an embryo before a woman may realize she's pregnant. Since more than half of pregnancies are unplanned, FDA has taken steps to fortify food so that all women of childbearing age get a daily dose of folic acid.

Without it, most women 19 to 50 get only 0.2 mg of folic acid each day, according to U.S. Department of Agriculture estimates. If the regulation is finalized within the next six months, FDA estimates that the fortified food will reach the plates of more than 90 percent of American women by 1995. If the move is successful in boosting women up to 0.4 mg of folic acid daily, it could cut the incidence of neural tube defects in this country by as much as half.

## A Difficult Decision

Despite this benefit, the decision to add folic acid to food is difficult because it's so tricky to estimate what people eat. Most of the folic acid studies have been done with vitamin pills, not plates of food. It's hard for scientists to translate the results of those controlled studies into recommendations for the ever changing eating habits of Americans.

"As a scientific and policy matter, it is one of the more difficult issues I have confronted," said FDA Commissioner David A. Kessler, M.D., addressing a meeting of the March of Dimes last January. "Before we fortify the food supply for 250 million Americans, we have to make sure we get it right."

The amount of folic acid FDA has proposed adding is tiny--40 micrograms per 100 grams (3.5 ounces) of bread and other grain products like flour, rolls, buns, corn grits, cornmeal, farina, rice, and noodles. (See February 1996 Fact Sheet for updated information.) A microgram is one millionth of a gram. This alone will probably not meet a woman's need for 0.4 mg (400 micrograms) each day, depending on what she eats. She will have to get the rest of her folic acid either from a vitamin supplement or from other foods in her diet. FDA is considering whether to allow food manufacturers to make health claims about which foods and vitamin supplements are rich in folic acid.

This is no problem for those who eat foods rich in folate. Leafy green vegetables, citrus fruits, beans, and fortified breakfast cereals are great folate sources. In fact, anyone who follows the USDA Food Pyramid Guide, which suggests 3 to 5 servings of vegetables, 2 to 4 of fruits and 6 to 11 servings of grains daily, can easily get 400 to 500 micrograms of folate each day.

The amount FDA is proposing be added to food is set below the level likely to cause harm from too much folate. A number of scientists believe that up to 1 mg (one-thousandth of a gram) of folic acid per day is safe. So even if someone followed USDA's guide, including eating fortified bread, and took a multivitamin with another 400 micrograms of folic acid, he or she would still be within safe limits.

The main problem is for older Americans. One in five people 65 to 95 lack sufficient vitamin B12, a deficiency that can cause pernicious anemia. Extra folic acid can mask the symptoms of the condition, which may lead to permanent nerve damage if left untreated.

FDA's proposal has drawn both support and criticism from a wide range of health officials and scientists. Experts in health and nutrition have taken opposite positions on the issue.

For instance, a working committee of scientists from the national Centers for Disease Control and Prevention in Atlanta wants FDA to require the addition of even more folic acid than proposed. The committee believes

the amount FDA has proposed is insufficient to prevent large numbers of neural tube defects.

"I've seen the trauma of neural tube defects. It's a very stressful situation for a family," says Joseph Mulinare, M.D., a pediatrician and medical epidemiologist at CDC. As a member of CDC's working group on folic acid, Mulinare and his colleagues would like to see FDA require two and a half times more folic acid in breads than it is considering.

On the other hand, other scientists have urged caution before fortifying the food supply. "I'm a little nervous about using large doses of folic acid," says James Mills, M.D., chief of pediatric epidemiology at the National Institute of Child Health and Human Development. "We don't really know what will happen if we add folic acid to the diets of 250 million people, and it may be difficult to identify any adverse effects."

Some nutritionists oppose fortification on principle, arguing that women can get all the folic acid they need from a well-balanced diet. And some consumer groups urged FDA to act sooner to prevent birth defects.

Since the Public Health Service recommended in 1992 that FDA require folic acid fortification, the agency has worked toward a policy that will reduce birth defects without harming anyone.

"FDA is criticized for being conservative, but in the area of uncertainty, it's best to be cautious," says Jeanne Rader, Ph.D., a biochemist with FDA's Office of Food Labeling. "If you err, you have to err on the side of caution."

## The No. 1 Disabling Birth Defect

There is good reason for health officials to seek to reduce the number of neural tube defects.

Neural tube malformations are serious birth defects that cause disability or death. They are the most common disabling birth defects, affecting between one and two infants out of every 1,000 births in the United States.

There are two main kinds of neural tube defects: anencephaly and spina bifida. A baby with anencephaly does not develop a brain, and dies shortly after birth.

Spina bifida is a defect of the spinal column. If the vertebrae (bones of the spinal column) surrounding the spinal cord do not close properly during the first 28 days after fertilization, the cord or spinal fluid bulge through, usually in the lower back.

While once all these children died, with proper medical treatment, about 85 to 90 percent of them now live to adulthood, according to the Spina Bifida Association of America. Depending on the severity of the condition, they have varying degrees of paralysis and incontinence.

There are two major forms of the condition. The mild form, spina bifida occulta ("hidden") is only a small gap in the spine, with a dimple in the skin covering it. There are usually no symptoms. Some Americans have spina bifida occulta and don't even know they have it, according to the National Information Center for Children and Youth with Disabilities.

The more disabling form is spina bifida aperta, which produces an noticeable sac on the infant's back. A small sac, called a meningocele, produces little or no muscle paralysis or incontinence once it is repaired.

But in 90 percent of all spina bifida cases, a portion of the undeveloped spinal cord itself protrudes through

the spine and forms a sac protruding on the baby's back. Any portion of the spinal cord outside the vertebrae is undeveloped or damaged, causing paralysis and incontinence. This is called a myelocele (or meningomyelocele), and it is what most people refer to as spina bifida.

The location of the sac determines how severely disabled the child will. In general, the higher it is on the spinal column, the more paralysis there is.

Doctors must repair the opening of the spine shortly after birth or the child will die. Other major surgeries often follow in the child's first years. About 85 percent of children with spina bifida develop hydrocephalus, an accumulation of cerebrospinal fluid surrounding the brain. This fluid must be drained to the abdomen or bloodstream with a surgically implanted tube.

Some children with spina bifida develop foot and knee deformities caused by an interruption of spinal nerve circuits. Many patients require leg braces, crutches, and other devices to help them walk. They may have learning disabilities, and about 30 percent of children have slight to severe mental retardation, especially if they have chronic hydrocephalus. Chronic bladder infections and kidney problems require lifelong medical attention.

Despite their need for medical attention, children with spina bifida can learn to care for many of their own needs. They often learn to catheterize themselves, for instance, so they can attend regular schools. With proper medical care, a person with spina bifida can live a long and productive life.

## Compelling Research

Scientists first hypothesized in the 1950s that diet had something to do with neural tube defects. The incidence of these conditions has always been higher in low socioeconomic populations in which women, presumably, have poorer diets. Also, babies conceived in the winter and early spring are more likely to be born with spina bifida, perhaps caused by a lack of fresh foods in early pregnancy.

In addition, researchers discovered in the 1960s that folic acid deficiency causes birth defects in animals. The nutrient plays an important role in cell division and growth.

But there appear to be factors other than nutrition in the development of spina bifida. Genetics also seems to play a role. People of Northern European and Hungarian ancestry have the highest rates of the disease, and the condition tends to run in families, although not consistently.

In fact, 90 to 95 percent of children with spina bifida are born to women who have no other children or anyone in their family with the defect.

In 1991, a study by British researchers found that women who already had one child with a neural tube defect could reduce by 72 percent the chance of another child being affected if they took high doses of folic acid.

Later studies showed that women with no history of giving birth to children with neural tube defects could reduce their risk by up to 60 to 75 percent if they took dietary supplements of between 0.4 mg and 0.8 mg of folic acid daily. The more folic acid the women took, the less was their chance of having a baby with a neural tube defect. One study also suggested that folate from food alone reduced the risk.

Scientists are in general agreement that folic acid reduces the risk of neural tube defects. What remains to be

seen is the effect it will have on the general population if it is added to breads and grains.

Historically, fortification with nutrients has produced good results. The United States has had success in fortifying bread with other B vitamins: riboflavin, niacin and thiamin, for example. Those nutrients were added to bread years ago and have virtually eliminated once common and serious diseases such as pellagra. Those vitamins were added in very small quantities, however. Whether bread fortified with higher doses of folic acid will work the same wonders without ill effects is not easy to determine.

Says FDA's Rader, "As a consumer, what you want is something that's going to be safe and effective, and that's not going to be dangerous, either.

"Fortifying the nation's food supply is not something where someone waves a magic wand and makes it happen. It's a very serious matter," she adds. "People think this is an easy decision, but it's not."

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# FOOD SOURCES OF FOLATE

| | Micrograms (per 100 g of food-3.5 oz) |
|---|---|
| dark-green leafy vegetables | 120-160 |
| other vegetables | 40-100 |
| fruits (particularly citrus) | 50-100 |
| beans (legumes) | 50-300 |
| whole grains | 60-120 |
| breakfast cereals | 100 or 400 |

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# Testing for Neural Tube Defects

A number of tests are available to diagnose neural tube defects before a baby is born.

One such test, the maternal serum alpha-fetoprotein (AFP) test, is a blood test for the mother at 16 to 18 weeks into the pregnancy. It was approved by FDA in the early 1980s as a prenatal test for neural tube defects (a second approved use is as an aid for a certain kind of testicular cancer).

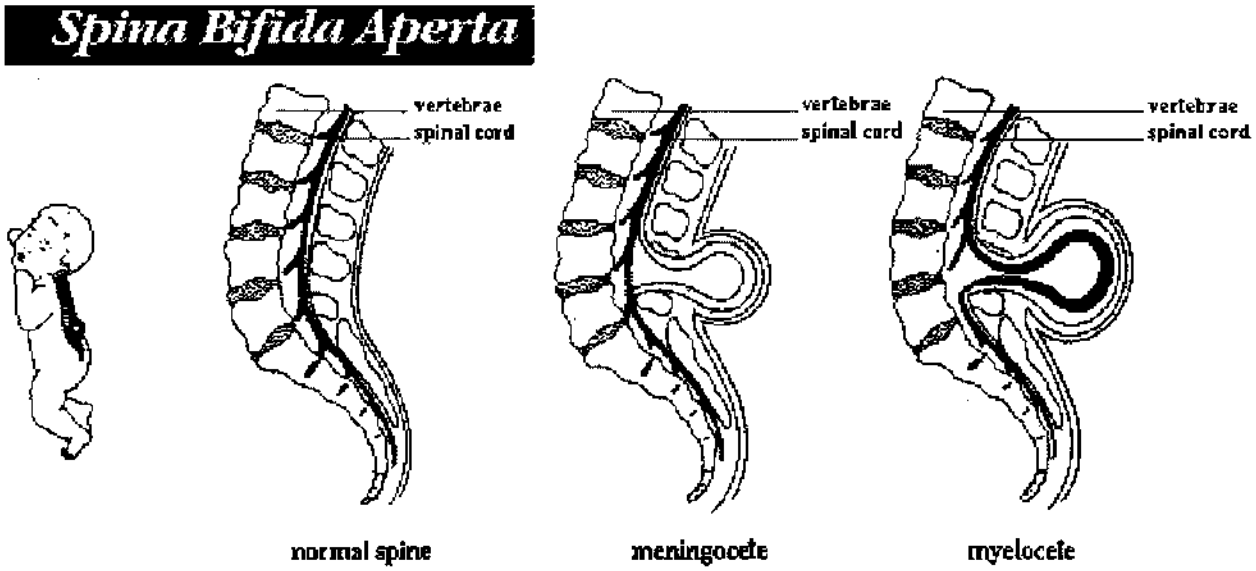
The test measures alpha-fetoprotein, a substance produced by the fetus and secreted into the amniotic fluid, eventually entering the mother's blood. As it grows, the baby produces increased amounts of AFP. The level of AFP in mother's blood peaks at about 30 to 32 weeks.

Abnormally high amounts of AFP may indicate a baby has a neural tube defect. But the test is not perfect.

Up to 20 percent of spina bifida cases do not produce high levels of AFP, so the test does not detect them. And when the test does indicate a high level of AFP, a neural tube defect is present only 10 percent of the time. Most commonly, the AFP level is high because the pregnancy is just further along than was thought.

Other possible causes of high AFP values are that the mother is carrying twins or that there is a placental problem. Women with diabetes or liver disease also have elevated AFP levels. Birth defects in the fetus such as kidney and heart problems may produce high AFP levels as well.

If a woman has an elevated AFP test, her doctor will usually give her a second AFP test, followed by ultrasound. If still no explanation for a high AFP value can be found, the physician may perform amniocentesis. In this test, the doctor takes a sample of the amniotic fluid and measures it for AFP levels. The results of these tests together will identify a high percentage of spina bifida cases.

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